Compounds recited in claim 11 have a fused benzene ring structure for the group represented by the A-ring structure set forth in claim 9. In that way, compounds of claim 11 would not include compounds of claim 9 having an A-ring selected from pyridine, cyclohexane or naphthalene. Clearly then, the subject matter of claim 11 further limits the scope of claim 9 and both claims are indeed proper.

Similarly, claim 13 was rejected as allegedly failing to further limit the scope of claim 12. Applicants respectfully disagree.

Claim 13 recites compounds of claim 12 further possessing specific activity against one or more specific indications. Specific biological activity is not a feature of the compounds set forth in claim 12. Clearly then, the subject matter of claim 13 further limits the scope of claim 12 and both claims are indeed proper.

Referring to the remaining §112 rejections noted in the Office Action, Applicants submit that the claims have been amended in order to address the noted informalities and other typographical errors. It is respectfully submitted that such amendments obviate the rejection.

Reconsideration and withdrawal of each of the §112 rejections are thus requested.

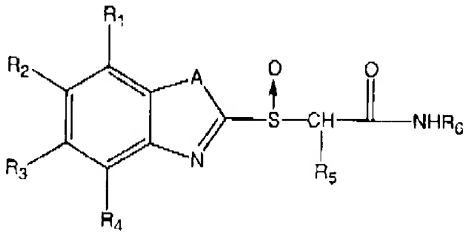
Claims 9-14 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hirai et al. [JP 04139172].

As the Office Action is understood, the position is taken that the cited documents report benzoxazole compounds which are allegedly related to Applicants' claimed subject matter.

The rejection is traversed.

The cited art neither teaches nor suggests Applicants' compounds of Formula I, pharmaceutical compositions comprising such compounds or therapeutic methods using such compounds.

For example, Hirai et al. recites certain alpha-sulfinyl-substituted acetamide derivatives of the formula:



wherein the benzoxazole sulfinyl group is linked to the amide group by a methylene linkage.

In contrast, the present invention provides compounds of Formula I where n is an integer of from 2 to 15, i.e., a 1,2-ethylene linkage or an α,ω-C_3-C_{15}-alkylene linkage. Compounds of the present invention now even exclude those compounds having a methylene linker, i.e., compounds of Formula I in which n is 1.

Additionally, Hirai reports compounds having gastric acid secretion inhibitory and anti-ulcer activity. In particular, the compounds provided by Hirai exhibit inhibitory activity against "H^+, K^+-ATPase" which is involved in the final stage of gastric acid secretion.

In contrast, compounds of the present invention have ACAT inhibitory activity which is involved in the formation of cholesterol ester. Indeed, ACAT is not even expressed in the stomach. Clearly then, one skilled in the art would not have found it obvious or even been motivated to prepare the compounds of the present invention in view of Hirai's disclosure of compounds which possess anti-ulcer activity.

Further, Hirai neither discloses nor suggests compounds of the instant invention, e.g., compounds having an alkylene linker with more than one carbon between the Y and Z group, or that it would be desirable for any such compounds to possess ACAT inhibitory activity.

Such structural distinction makes clear that a *prima facie* case of obviousness is not presented by Hirai. Much greater structural similarity has been required to sustain a Section 103 rejection. For example, in *In re Grabiak*, 226 USPQ 872, the Court of Appeals for the Federal Circuit reversed a Section 103 rejection on the basis that the prior art provided no suggestion to replace oxygen (in an ester of the prior art compound) with a sulfur (to provide the thioester of the claimed compound). The Federal Circuit particularly noted (page 872):

> The PTO cited no pertinent reference showing or suggesting to one of ordinary skill in the art the change of a thioester for an ester group. In the absence of such reference, there is inadequate support for the PTO's position that this modification would *prima facie* have been obvious.

Clearly then, Hirai's disclosure is deficient and cannot sustain the instant rejection. Accordingly, reconsideration and withdrawal of the §103 rejection are thus requested.

It is believed that the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

May 16, 2002

Peter F. Corless (Reg. No. 33860)
John B. Alexander (Reg. No.: 48399)
Dike, Bronstein, Roberts & Cushman IP Group
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209
Tel. (617) 439-4444

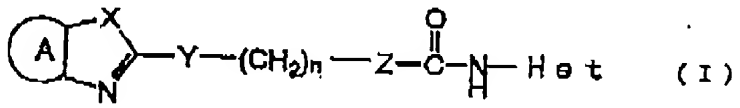
VERSION MARKED TO SHOW CHANGES

(Additions are underlined; deletions are bracketed.)

IN THE CLAIMS

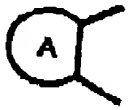
Claims 9-13 and 15-18 have been amended as follows:

9. (amended) Compounds represented by the formula (I)

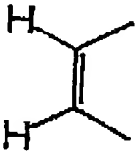


(I)

wherein



represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

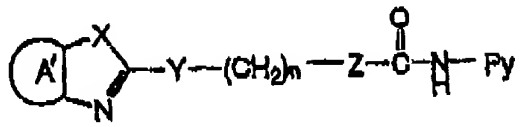
Y represents -NR_4 -, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from [1]2 to 15 [(except that n is 1)], or salts or solvates thereof.

10. (amended) The compounds according to claim 9, which are represented by the formula (IA)



(I A)

wherein

represents an optionally substituted divalent residue of benzene or pyridine;

Py represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR_4[,]-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

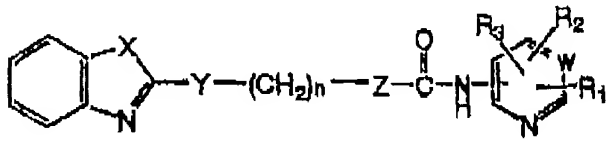
Z represents a single bond;

R_4[,] represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from [1]2 to 15 [(except that n is 1)];

or salts or solvates thereof.

11. (amended) The compounds according to claim 9, which are represented by the formula (III)



(III)

wherein, W represents =CH-;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR_4-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

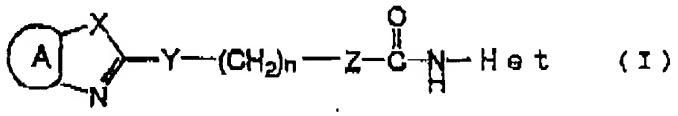
Z represents a single bond;

R_1, R_2, and R_3[,] are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group, provided [(except] that R_1, R_2 and R_3[, all] are [a]not hydrogen at the same time[)];

R_4[,] represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from [1]2 to 15 [(except that n is 1)], or salts or solvates thereof.

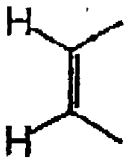
12. (amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound selected from the compounds represented by the formula (I)



(I)

wherein

represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR[,]-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

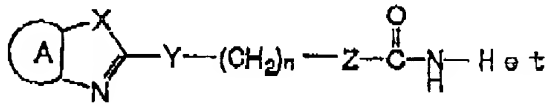
Z represents a single bond;

R_4[,] represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from [1]2 to 15 [(except that n is 1)], or salts or solvates thereof.

13. (amended) The pharmaceutical composition according to claim 12, which is an ACAT inhibitor, an intracellular cholesterol[,] transfer inhibitor, a blood cholesterol depressant or a macrophage foamation suppressant.

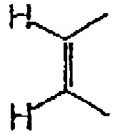
15. (amended) The method for treating hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm in need of such treatment [using] by administering a compound[s] of the formula (I')



(I')

wherein

represents an optionally substituted divalent residue of benzene, pyridine, cyclohexane or naphthalene, or a group:



;

Het represents substituted or unsubstituted pyridyl or pyrimidyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR_4[,]-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

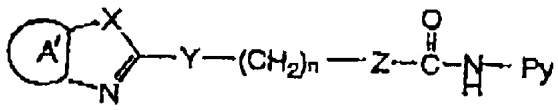
Z represents a single bond;

R_4[,] represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

16. (amended) The method of claim 15 wherein a [using] compound[s] of [the] formula (I'A) is administered



(I'A)

wherein

represents an optionally substituted divalent residue of benzene or pyridine;

Py represents an optionally substituted pyridyl or pyrimidyl group;

X represents -NH-, an oxygen atom or a sulfur atom;

Y represents $-NR_4-$, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

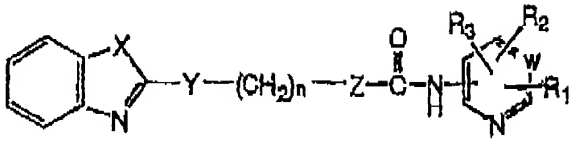
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group;

n is an integer of from 1 to 15,

or salts or solvates thereof.

17. (amended) The method of claim 15 [using] wherein a compound[s] of [the] formula (III') is administered



(III')

wherein, w represents =CH- or =N-,

x represents -NH-, an oxygen atom or a sulfur atom;

Y represents -NR_4- an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

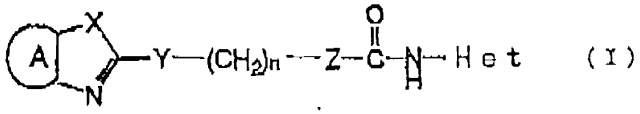
R_1, R_2, and R_3[,] are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group;

R_4[,] represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

18. (amended) A method claim 15 [using] <u>wherein</u> a compound represented by [the] formula (I) <u>is administered</u>, [wherein]



(I)

wherein

represents an optionally substituted divalent residue of benzene;

Het represents a substituted or unsubstituted pyridyl group;

X is an oxygen atom;

Y is a sulfur atom;

Z is a single bond;

n is 1;

or salts or solvates thereof.